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L48  ANSWER 1 OF 6  HCAPLUS  COPYRIGHT 2003 ACS
AN   2003:5673  HCAPLUS
DN   138:66677
TI   Blocking peptide for inflammatory cell secretion, and therapeutic use
IN   Martin, Linda; Adler, Kenneth B.; Li, Yuehua
PA   North Carolina State University, USA
SO   PCT Int. Appl., 54 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
ICI  A61
CC   1-7 (Pharmacology)
     Section cross-reference(s): 14
FAN.CNT 1
     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ----------------  ----  --------      ---------------  --------
PI   WO 2003000027     A2    20030103      WO 2002-US22270  20020626
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
           CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
           GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
           LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
           PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
           UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
           TJ, TM
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
           CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MN, NL, PT, SE, TR,
           BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     US 2003013652     A1    20030116      US 2002-180753   20020626
PRAI US 2001-300933P   P     20010626
AB   The invention includes methods of modulating cellular secretory processes.
     More specifically, the invention relates to modulating the release of
     inflammatory mediators.  Addnl., the invention discloses an intracellular
     signaling mechanism that regulates airway mucin secretion as well as
     illustrating several intracellular targets for pharmacol. intervention in
     disorders involving aberrant secretion of respiratory mucins and/or
     secretion of inflammatory mediators from membrane-bound vesicles.
ST   blocking peptide inflammatory cell secretion therapeutic; inflammation
     mediator release modulation peptide; respiratory mucin secretion
     therapeutic peptide
IT   Intestine, disease
        (Crohn's; blocking peptide for inflammatory cell secretion, and
        therapeutic use)
IT   Proteins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (MANS; blocking peptide for inflammatory cell
        secretion, and therapeutic use)
IT   Peptides, biological studies
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (MANS; blocking peptide for inflammatory cell
```

secretion, and therapeutic use)
IT Actins
Myosins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**MARCKS** assocn. with; blocking **peptide** for inflammatory cell secretion, and therapeutic use)
IT Animal cell line
(NHBE; blocking peptide for inflammatory cell secretion, and therapeutic use)
IT Drug delivery systems
(aerosols; blocking peptide for inflammatory cell secretion, and therapeutic use)
IT Anti-inflammatory agents
Antiarthritics
Antiasthmatics
Arthritis
Asthma
Cat (Felis catus)
Cystic fibrosis
Dephosphorylation, biological
Dog (Canis familiaris)
Drug delivery systems
Eczema
Exocytosis
Horse (Equus caballus)
Human
Inflammation
Psoriasis
Secretion (process)
(blocking peptide for inflammatory cell secretion, and therapeutic use)
IT **MARCKS (myristoylated alanine-rich C kinase substrate)**
Mucins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(blocking **peptide** for inflammatory cell secretion, and therapeutic use)
IT Antibiotics
Antiviral agents
Immunosuppressants
Parasiticides
(blocking peptide for inflammatory cell secretion, therapeutic use, and use with other agents)
IT Bronchi
(chronic bronchitis; blocking peptide for inflammatory cell secretion, and therapeutic use)
IT Lung, disease
(chronic obstructive; blocking peptide for inflammatory cell secretion, and therapeutic use)
IT Respiratory tract
(disease, inflammation from; blocking peptide for inflammatory cell secretion, and therapeutic use)
IT Drugs
(gastrointestinal; blocking peptide for inflammatory cell secretion, and therapeutic use)
IT Organelle
(granule, mucin; blocking peptide for inflammatory cell secretion, and therapeutic use)
IT Pain
(inflammation from pain syndromes; blocking peptide for inflammatory cell secretion, and therapeutic use)
IT Autoimmune disease
Intestine, disease
Skin, disease

(inflammation from; blocking peptide for inflammatory cell secretion, and therapeutic use)

IT Basophil
Eosinophil
Leukocyte
Monocyte
Neutrophil
(inflammatory mediators produced by; blocking peptide for inflammatory cell secretion, and therapeutic use)

IT Drug delivery systems
(inhalants; blocking peptide for inflammatory cell secretion, and therapeutic use)

IT Medical goods
(inhalers, dry powder and metered dose; blocking peptide for inflammatory cell secretion, and therapeutic use)

IT Intestine, disease
(irritable bowel syndrome; blocking peptide for inflammatory cell secretion, and therapeutic use)

IT Signal transduction, biological
(mucin secretion regulation; blocking peptide for inflammatory cell secretion, and therapeutic use)

IT Drug delivery systems
(nasal; blocking peptide for inflammatory cell secretion, and therapeutic use)

IT Drug delivery systems
(oral; blocking peptide for inflammatory cell secretion, and therapeutic use)

IT Drug delivery systems
(parenterals; blocking peptide for inflammatory cell secretion, and therapeutic use)

IT Phosphorylation, biological
(protein; blocking peptide for inflammatory cell secretion, and therapeutic use)

IT Drug delivery systems
(pulmonary; blocking peptide for inflammatory cell secretion, and therapeutic use)

IT Drug delivery systems
(rectal; blocking peptide for inflammatory cell secretion, and therapeutic use)

IT Skin, disease
(rosacea; blocking peptide for inflammatory cell secretion, and therapeutic use)

IT Mucus
(secretion; blocking peptide for inflammatory cell secretion, and therapeutic use)

IT Acne
(severe; blocking peptide for inflammatory cell secretion, and therapeutic use)

IT Drug delivery systems
(topical; blocking peptide for inflammatory cell secretion, and therapeutic use)

IT Intestine, disease
(ulcerative colitis; blocking peptide for inflammatory cell secretion, and therapeutic use)

IT 479482-23-0
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(blocking peptide for inflammatory cell secretion, and therapeutic use)

IT 141436-78-4, Protein kinase C 141588-27-4, Protein kinase G 362674-81-5, Protein phosphatase 2a
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(mucin secretion in relation to; blocking peptide for inflammatory cell secretion, and therapeutic use)

IT 480430-49-7
RL: PRP (Properties)
(unclaimed sequence; blocking peptide for inflammatory cell secretion, and therapeutic use)

L48 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2003 ACS
AN 2001:846313 HCAPLUS
DN 136:99693
TI **MARCKS protein** is a key molecule regulating mucin secretion by human airway epithelial cells in vitro
AU **Li, Yuehua; Martin, Linda D.**; Spizz, Gwendolyn; **Adler, Kenneth B.**
CS Department of Anatomy, Physiological Sciences and Radiology, College of Veterinary Medicine, North Carolina State University, Raleigh, NC, 27606, USA
SO Journal of Biological Chemistry (2001), 276(44), 40982-40990
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
CC 13-2 (Mammalian Biochemistry)
AB Hypersecretion of airway mucin characterizes numerous respiratory diseases. Although diverse pathol. stimuli can provoke exocytotic release of mucin from secretory cells of the airway epithelium, mechanisms involved remain obscure. This report describes a new paradigm for the intracellular signaling mechanism regulating airway mucin secretion. Direct evidence is provided that the **myristoylated alanine-rich C kinase substrate** (**MARCKS**) is a central regulatory mol. linking secretagogue stimulation at the cell surface to mucin granule release by differentiated normal human bronchial epithelial cells in vitro. Down-regulation of **MARCKS** expression or disruption of **MARCKS** function in these cells inhibits the secretory response to subsequent stimulation. The intracellular mechanism controlling this secretory process involves cooperative action of two sep. protein kinases, protein kinase C and cGMP-dependent protein kinase. Upon stimulation, activated **protein** kinase C phosphorylates **MARCKS**, causing translocation of **MARCKS** from the plasma membrane to the cytoplasm, where it is then dephosphorylated by a **protein** phosphatase 2A that is activated by cGMP-dependent **protein** kinase, and assocs. with both actin and myosin. Dephosphorylated cytoplasmic **MARCKS** would also be free to interact with mucin granule membranes and thus could link granules to the contractile cytoskeleton, mediating their movement to the cell periphery and subsequent exocytosis. These findings suggest several novel intracellular targets for pharmacol. intervention in disorders involving aberrant secretion of respiratory mucin and may relate to other lesions involving exocytosis of membrane-bound granules in various cells and tissues.
ST **MARCKS** G C kinase mucin secretion airway epithelium
IT Cytoplasm
(**MARCKS** assocs. with actin and myosin in regulating mucin secretion by human airway epithelial cells in vitro)
IT Actins
Myosins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**MARCKS** assocs. with actin and myosin in regulating mucin secretion by human airway epithelial cells in vitro)
IT Secretion (process)
(**MARCKS protein** is key mol. regulating mucin secretion by human airway epithelial cells in vitro)
IT **MARCKS (myristoylated alanine-rich C kinase substrate)**
Mucins

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**MARCKS protein** is key mol. regulating mucin secretion by human airway epithelial cells in vitro)

IT Respiratory tract
(epithelium; **MARCKS protein** is key mol. regulating mucin secretion by human airway epithelial cells in vitro)

IT 141436-78-4, **Protein** kinase C 141588-27-4, **Protein** kinase G
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**MARCKS** regulation of mucin secretion by human airway epithelial cells involves activation of **protein** kinases C and G)

RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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L48 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2003 ACS
AN 2001:697269 HCAPLUS
DN 136:115748
TI **MARCKS protein**: A potential modulator of airway mucin secretion
AU **Li, Yuehua; Martin, Linda D.; Adler, Kenneth B.**
CS College of Veterinary Medicine, North Carolina State University, Raleigh, NC, USA
SO Cilia and Mucus: From Development to Respiratory Defense, [International Meeting], 2nd, Sirmione, Italy, Nov. 3-4, 1999 (2001), Meeting Date 1999, 179-193. Editor(s): Salathe, Matthias. Publisher: Marcel Dekker, Inc., New York, N. Y.
CODEN: 69BVC5
DT Conference; General Review
LA English
CC 13-0 (Mammalian Biochemistry)
AB A review on **myristoylated alanine-rich C kinase substrate protein**, and on a rationale for looking at **MARCKS protein** as a

potentially important regulator of airway mucin secretion. **MARCKS protein** was identified as a specific in vitro and in vivo substrate for **protein** kinase C. The preliminary study of a potential role for **MARCKS protein** in the process of airway mucin secretion showed that it is involved in the secretory pathway and could be a major convergent mol. in intracellular signaling leading to mucin granule transport and exocytosis in human globlet cells in vitro.

ST review **MARCKS protein** mucin airway

IT Respiratory tract
(**MARCKS protein**: A potential modulator of airway mucin secretion)

IT **MARCKS** (**myristoylated alanine-rich C kinase substrate**)
Mucins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**MARCKS protein**: A potential modulator of airway mucin secretion)

RE.CNT 81 THERE ARE 81 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L48 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2003 ACS
AN 2000:750090 HCAPLUS
DN 133:347833
TI **MARCKS protein**, a key intracellular molecule controlling mucin secretion by human airway epithelial cells
AU **Li, Yuehua**
CS North Carolina State Univ., NC, USA
SO (1999) 100 pp. Avail.: UMI, Order No. DA9960139
From: Diss. Abstr. Int., B 2000, 61(2), 639-640
DT Dissertation
LA English
CC 13-2 (Mammalian Biochemistry)
AB Unavailable
ST **MARCKS protein** mucin secretion airway epithelium
IT **MARCKS (myristoylated alanine-rich C kinase substrate)**
Mucins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**MARCKS protein**, key intracellular mol. controlling mucin secretion by human airway epithelial cells)
IT Respiratory tract
(epithelium; **MARCKS protein**, key intracellular mol. controlling mucin secretion by human airway epithelial cells)
IT Secretion (process)

(**protein; MARCKS protein**, key intracellular mol. controlling mucin secretion by human airway epithelial cells)

L48 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2003 ACS
AN 2000:608596 HCAPLUS
DN 133:187988
TI Methods and compositions for altering mucus secretion
IN **Li, Yuehua; Martin, Linda D.; Adler, Kenneth B.**
PA North Carolina State University, USA
SO PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DT Patent
LA English
IC A61K038-17; A61K031-7088; A61K031-35; A61K031-00; A61K009-72; A61K091-27; C07H021-00; G01N033-50; A61K038-19; A61K031-739; A61P011-00; A61P001-00
CC 1-12 (Pharmacology)
Section cross-reference(s): 15, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000050062	A2	20000831	WO 2000-US5050	20000224
	WO 2000050062	A3	20001221		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1154786	A2	20011121	EP 2000-912034	20000224
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002538783	T2	20021119	JP 2000-600672	20000224
PRAI	US 1999-256154	A	19990224		
	WO 2000-US5050	W	20000224		

AB Methods and compds. for increasing or decreasing mucus secretion in subjects, and particularly mucus secretion in the airways, are described. The use of compds. that modulate **MARCKS protein** -related mucus secretion is described. Methods of screening compds. for the ability to increase or decrease mucus secretion are also described.
ST mucus secretion modulator **MARCKS protein**
IT Antisense oligonucleotides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**MARCKS protein**-directed; methods and compns. for altering **MARCKS protein**-related mucus secretion)
IT Gene, animal
mRNA
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**MARCKS protein**-encoding, antisense oligonucleotides to; methods and compns. for altering **MARCKS protein**-related mucus secretion)
IT Drug delivery systems
(aerosols; methods and compns. for altering **MARCKS protein**-related mucus secretion)
IT Bronchi
(bronchitis, inhibition of mucus secretion in; methods and compns. for altering **MARCKS protein**-related mucus secretion)

IT Lung, disease
(chronic obstructive, inhibition of mucus secretion in; methods and compns. for altering **MARCKS protein**-related mucus secretion)
IT Eye
(conjunctiva; methods and compns. for altering **MARCKS protein**-related mucus secretion)
IT Bronchi
(epithelium; methods and compns. for altering **MARCKS protein**-related mucus secretion)
IT Receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(for **MARCKS protein**, on mucin granule; methods and compns. for altering **MARCKS protein**-related mucus secretion)
IT Asthma
Common cold
Cystic fibrosis
Emphysema
Influenza
Pneumonia
(inhibition of mucus secretion in; methods and compns. for altering **MARCKS protein**-related mucus secretion)
IT Drug delivery systems
(liposomes; methods and compns. for altering **MARCKS protein**-related mucus secretion)
IT Drug delivery systems
Drug screening
Mucous membrane
Mucus
(methods and compns. for altering **MARCKS protein** -related mucus secretion)
IT **MARCKS (myristoylated alanine-rich C kinase substrate)**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(methods and compns. for altering **MARCKS protein** -related mucus secretion)
IT Calmodulins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and compns. for altering **MARCKS protein** -related mucus secretion)
IT Cytokines
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and compns. for altering **MARCKS protein** -related mucus secretion)
IT Lipopolysaccharides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and compns. for altering **MARCKS protein** -related mucus secretion)
IT **Peptides**, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and compns. for altering **MARCKS protein**

-related mucus secretion)

IT Tumor necrosis factors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and compns. for altering **MARCKS protein** -related mucus secretion)

IT Digestive tract
Respiratory tract
Respiratory tract
Vagina
Vagina
(mucosa; methods and compns. for altering **MARCKS protein**-related mucus secretion)

IT Urogenital tract
(mucous membrane; methods and compns. for altering **MARCKS protein**-related mucus secretion)

IT Mucous membrane
Mucous membrane
(respiratory tract; methods and compns. for altering **MARCKS protein**-related mucus secretion)

IT Nose
(rhinitis, inhibition of mucus secretion in; methods and compns. for altering **MARCKS protein**-related mucus secretion)

IT Organelle
(secretory granule, mucin granule, **MARCKS protein** binding site on; methods and compns. for altering **MARCKS protein**-related mucus secretion)

IT Antibodies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(to **MARCKS protein**; methods and compns. for altering **MARCKS protein**-related mucus secretion)

IT Mucous membrane
Mucous membrane
(vaginal; methods and compns. for altering **MARCKS protein**-related mucus secretion)

IT 108068-98-0, KT 5720
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(KT 5720; methods and compns. for altering **MARCKS protein**-related mucus secretion)

IT 289643-18-1
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(amino acid sequence, fragments; methods and compns. for altering **MARCKS protein**-related mucus secretion)

IT 63-39-8, Uridine 5'-triphosphate 16561-29-8, PMA 21870-09-7 78111-17-8, Okadaic acid 91300-60-6, LY83583 121263-19-2, Calphostin C 134248-85-4 289470-83-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and compns. for altering **MARCKS protein** -related mucus secretion)

IT 140342-87-6, 4: PN: WO0050062 SEQID: 3 unclaimed DNA 144559-94-4
RL: PRP (Properties)
(unclaimed nucleotide sequence; methods and compns. for altering mucus secretion)

IT 148769-19-1, Protein 80K-L (human clone .lambda.80L-1 gene MACS reduced)
RL: PRP (Properties)
(unclaimed protein sequence; methods and compns. for altering mucus

secretion)

L48 ANSWER 6 OF 6 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2000:302905 BIOSIS
DN PREV200000302905
TI **Myristoylated alanine-rich C-kinase substrate** protein: A major intracellular regulatory molecule controlling secretion of mucin by human airway goblet cells.
AU **Adler, Kenneth B. (1); Li, Y.; Martin, L. D.**
CS (1) College of Veterinary Medicine, North Carolina State University, 4700 Hillsborough St, Raleigh, NC, 27606 USA
SO Chest, (May, 2000) Vol. 117, No. 5 Suppl. 1, pp. 266S-267S. print.
Meeting Info.: 42nd Annual Thomas L. Petty Lung Conference: Mechanisms of COPD San Francisco, California, USA October 22-26, 2000
ISSN: 0012-3692.
DT Conference
LA English
SL English
CC Respiratory System - General; Methods *16001
Cytology and Cytochemistry - Human *02508
Biophysics - General Biophysical Studies *10502
Enzymes - General and Comparative Studies; Coenzymes *10802
Metabolism - General Metabolism; Metabolic Pathways *13002
General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
BC Hominidae 86215
IT Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology; Metabolism; Respiratory System (Respiration)
IT Parts, Structures, & Systems of Organisms
airway goblet cell: respiratory system
IT Chemicals & Biochemicals
mucin: airway goblet cell secretion; **myristoylated alanine-rich C-kinase substrate** protein: major intracellular regulatory molecule
IT Miscellaneous Descriptors
Meeting Abstract
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae)
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

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FILE 'WPIX' ENTERED AT 08:03:15 ON 11 MAY 2003
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FILE LAST UPDATED: 5 MAY 2003 <20030505/UP>
MOST RECENT DERWENT UPDATE: 200329 <200329/DW>
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=> d all abeq tech abex tot

L54 ANSWER 1 OF 2 WPIX (C) 2003 THOMSON DERWENT
AN 2003-278239 [27] WPIX
DNC C2003-072601
TI Method of regulating inflammation comprises administering a composition comprising a **MANS peptide** or an active fragment thereof.
DC B04 C03
IN **ADLER, K B; LI, Y; MARTIN, L D**
PA (UYNC-N) UNIV NORTH CAROLINA STATE
CYC 100
PI WO 2003000027 A2 20030103 (200327)* EN 51p C07K000-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
ADT WO 2003000027 A2 WO 2002-US22270 20020626
PRAI US 2001-300933P 20010626
IC ICM C07K000-00
AB WO2003000027 A UPAB: 20030429
NOVELTY - Method of regulating inflammation comprises administering a composition comprising a **MANS peptide** or an active fragment thereof.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1) a method of regulating a cellular secretory process comprising administering a compound comprising a **MANS peptide** or fragment thereof that regulates an inflammatory mediator;
(2) a method of reducing inflammation comprising administering a compound that inhibits the **MARCKS**-related release of inflammatory mediators, whereby mucus secretion is reduced;
(3) a method of reducing inflammation comprising administering a compound that inhibits the **MARCKS**-related release of inflammatory mediators;
(4) a method of regulating (i.e. reducing) mucin granule release;
(5) a method of regulating exocytotic secretion of airway mucin granules by administering a compound that regulates mucin granule release;
(6) a method of modulating (i.e. inhibiting) mucus secretion comprising administering an antisense sequence that is complementary to sequences encoding a **MARCKS protein** or an active fragment thereof; and
(7) a method of reducing or inhibiting inflammation by administering a **MANS peptide** or an active fragment thereof to modulate an inflammatory mediator at the inflammation site.
ACTIVITY - Antiinflammatory; Respiratory; Antiasthmatic; Gastrointestinal; Antiulcer; Dermatological; Antipsoriatic; Antiseborrheic; Antiarthritic; Immunosuppressive; Analgesic.
No supporting data given.
MECHANISM OF ACTION - None given.

USE - For treating inflammation caused by respiratory diseases (e.g. asthma, chronic bronchitis and chronic obstructive pulmonary disease (COPD), bowel diseases (e.g. irritable bowel syndrome, Crohn's disease and ulcerative colitis), skin diseases (e.g. rosacea, eczema, psoriasis and severe acne), autoimmune diseases and pain syndromes, arthritis and cystic fibrosis (claimed).

ADVANTAGE - Inhibits both mucus secretion and inflammatory mediators.

Dwg.0/15

FS CPI

FA AB; DCN

MC CPI: B02-Z; B04-C01; B04-E06; B04-N02A; B14-A02; B14-B02; B14-C01; B14-C03; B14-C09; B14-E08; B14-E10C; B14-G02; B14-G02D; B14-K01A; B14-K01D; B14-L06; B14-N17; C02-Z; C04-C01; C04-E06; C04-N02A; C14-A02; C14-B02; C14-C01; C14-C03; C14-C09; C14-E08; C14-E10C; C14-G02; C14-G02D; C14-K01A; C14-K01D; C14-L06; C14-N17

TECH UPTX: 20030429

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred **Peptide**: Active fragment of the **MANS protein** comprises at least 6 amino acids. Antisense sequence is at least 18 nucleic acids in length. Inflammatory mediators are produced by cells selected from neutrophils, basophils, eosinophils, monocytes and leukocytes.

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: Compositions further comprise a second molecule selected from antibiotics, antivirals, antiparasitics, antiinflammatories and immunosuppressants.

ABEX UPTX: 20030429

ADMINISTRATION - Administration is topically, parenterally, rectally, pulmonarily (by aerosol, dry powder inhaler, metered dose inhaler or nebulizer), nasally, orally or by inhalation to humans, canines, equines and felines (claimed). No dosage given.

L54 ANSWER 2 OF 2 WPIX (C) 2003 THOMSON DERWENT

AN 2000-572036 [53] WPIX

DNN N2000-423201 DNC C2000-170513

TI Regulating mucus secretion by a mucus-secreting cell, useful for treating e.g. bronchitis, asthma or pneumonia, by administering a compound that inhibits or enhances **myristolated alanine-rich C-kinase substrate** protein.

DC B04 S03

IN **ADLER, K B; LI, Y; MARTIN, L D**

PA (UYNC-N) UNIV NORTH CAROLINA STATE

CYC 87

PI WO 2000050062 A2 20000831 (200053)* EN 66p A61K038-17

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW

W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW

AU 2000033833 A 20000914 (200063) A61K038-17

EP 1154786 A2 20011121 (200176) EN A61K038-17

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

JP 2002538783 W 20021119 (200281) 76p C12N015-09

ADT WO 2000050062 A2 WO 2000-US5050 20000224; AU 2000033833 A AU 2000-33833 20000224; EP 1154786 A2 EP 2000-912034 20000224, WO 2000-US5050 20000224; JP 2002538783 W JP 2000-600672 20000224, WO 2000-US5050 20000224

FDT AU 2000033833 A Based on WO 200050062; EP 1154786 A2 Based on WO 200050062; JP 2002538783 W Based on WO 200050062

PRAI US 1999-256154 19990224

IC ICM A61K038-17; C12N015-09

ICS A61K009-127; A61K009-72; A61K031-00; A61K031-35; A61K031-7088; A61K031-739; A61K038-00; A61K038-19; A61K048-00; A61P001-00;

A61P011-00; A61P011-10; A61P043-00; C07H021-00; C12Q001-02; G01N033-15; G01N033-50; G01N033-53

ICA C07K014-47; C07K016-18; C12N005-06

AB WO 200050062 A UPAB: 20001023

NOVELTY - Inhibiting or increasing mucus secretion by a mucus-secreting cell comprises administering a compound that inhibits or enhances **myristolated alanine-rich C-kinase substrate (MARCKS) protein**, where mucus secretion by the cell is reduced or enhanced compared to that which would occur in the absence of the compound.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) methods of inhibiting mucus secretion by a mucus-secreting cell comprises administering to the cell a mucus-inhibitory compound that inhibits **MARCKS protein**-related mucus secretion, where mucus secretion by the cell is reduced compared to that which would occur in the absence of the compound;

(2) methods of enhancing mucus secretion by a mucus-secreting cell by administering a secretion-enhancing fragment of a **MARCKS protein** or a compound that binds to an endogenous inhibitor of **MARCKS protein**, where the amount of mucus secreted is increased compared to that which would occur in the absence of the **protein** fragment or the compound;

(3) an oligonucleotide having a sequence of 10-50 nucleotides that hybridizes to the nucleotide molecules encoding a **MARCKS protein** under physiologic conditions and where the oligonucleotide inhibits expression of the **MARCKS protein** when administered to a cell containing the endogenous nucleotide molecules;

(4) methods of inhibiting mucus secretion by a mucus-secreting cell by administering a mucus inhibitory compound that binds to a target site which may be the mucin granule membranes at the site bound by **MARCKS protein** or the **MARCKS protein** at the mucin granule binding site; and

(5) a method of screening for the ability to bind in a mucus-secreting cell to a site which may be mucin granule membranes at the site bound by **MARCKS protein** or a **MARCKS protein** at the mucin granule membrane binding site, comprising administering the test compound to a mucus-secreting cell and then detecting whether the test compound inhibits binding of endogenous **MARCKS protein** to the mucin granule membrane.

ACTIVITY - Anti-inflammatory; anti-asthmatic; virucide; antibacterial.

No clinical data given.

MECHANISM OF ACTION - **Myristolated alanine-rich C-kinase substrate** phosphorylation inhibitor; **myristolated alanine-rich C-kinase substrate** dephosphorylation inhibitor.

USE - The methods and compositions are useful in regulating mucus secretion, and in treating medical conditions where it is desirable to increase or decrease mucus secretion, such as bronchitis, asthma, cystic fibrosis, chronic obstructive pulmonary disease (COPD), emphysema, pneumonia, influenza, or rhinitis. These may be used to inhibit or reduce mucus secretion occurring from any mucus-secreting cell, such as goblet cells, or tissue, such as mucous membranes of the airways, to block the secretion of inflammatory mediators from cells such as macrophages, neutrophils and mast cells. The mucus-inhibitory compounds may have a dual function of decrease mucus secretion and inflammation. Methods of reducing airway mucus secretion would also be useful for treating bacterial or viral infections, e.g. pneumonia, influenza and the common cold, and in animals, such methods are further used in treating kennel cough and equine COPD (undefined).

ADVANTAGE - The new methods and compounds differ from the prior

treatments of reducing mucus secretion, e.g. steroid treatments or antihistamines, in that cellular secretion of mucus in response to a variety of stimuli is directly blocked at the cellular level.
Dwg.0/12
FS CPI EPI
FA AB; DCN
MC CPI: B04-C01; B04-E03; B04-E06; B04-F01; B04-L04; B04-M01; B04-N04; B11-C09; B12-M01A; B12-M02; B14-A01; B14-A02; B14-C03; B14-K01A; B14-L01; B14-L06
EPI: S03-E14H
TECH UPTX: 20001023
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Compounds: The mucus inhibiting compound is an active fragment of a **MARCKS protein** or an antisense compound directed against endogenous nucleotide molecules that encode a **MARCKS protein**. The active fragment is a **peptide** comprising a sequence of 10-50 contiguous amino acids encoded by a fully defined 1885-base pair (bp) sequence, is an N-terminal sequence of a **MARCKS protein** , preferably myristolated. The compound may also be an okadaic acid, calphostin C, Rp-8-Br-cGMP or LY83583. Inhibiting mucus secretion comprises administering a **peptide** inhibitor of **MARCKS** -related mucus secretion, where the **peptide** comprises a sequence of 24 or 25 amino acids given in the specification. The mucus-enhancing compound is myristolated and comprised of 10-50 contiguous amino acids from a phosphorylation site domain of a **MARCKS protein** . The compound is preferably calmodulin. The compound, which can stimulate mucus secretion, is uridine 5'-triphosphate, phorbol 12-myristate 13-acetate, or 8-bromo-cGMP. The compound may also be a cytokine, tumor necrosis factor-alpha, or lipopolysaccharide. The compound to be tested for its ability to inhibit binding of endogenous **MARCKS protein** to the mucin granule membrane is a **peptide** fragment of a **MARCKS protein** or its analog, or an antibody that specifically binds to **MARCKS protein**.
The test compound is preferably labeled with a detectable molecule.
Preferred Cell: The mucus-secreting cell is an epithelial cell contained within airway, gastrointestinal or ocular mucous membranes, or genitourinary membranes. The cells used for testing a compound for its ability to inhibit binding of endogenous **MARCKS protein** to the mucin granule membrane are normal bronchial epithelial cells.
ABEX UPTX: 20001023
SPECIFIC SEQUENCES - The mucus secretion-inhibiting peptide is a myristolated polypeptide having the sequence:
GAQFSKTAAKGEAAAERPGEAAVA
The mucus secretion-enhancing peptide has the sequence:
KKKKKRFSRKKSFKLSGFSFKKNKK

ADMINISTRATION - The mucus-inhibiting compound is administered to the gastrointestinal tract or to the airways of a subject suffering from bronchitis, asthma, cystic fibrosis, chronic obstructive pulmonary disease, emphysema, pneumonia, influenza, rhinitis or common cold by inhalation or via aerosol administration to the lungs. The mucus secretion-enhancing fragment of a **MARCKS protein** is administered to the eye or to the vaginal epithelium. The antisense construct is introduced into the cells in a liposome (all claimed). Pharmaceutical compositions may also be administered through rectal, or topical (including buccal, dermal and ocular) routes.
EXAMPLE - Culture normal human bronchial epithelial cells were co-incubated for 15 minutes in apical and basolateral media containing 1, 10, or 100 muM of **MANS peptide**, and then co-incubated for 15 minutes with the **peptide** and 100 nM phorbol 12-myristate 13-acetate (PMA) plus 1 muM 8-bromo-cGMP (cGMP). Stimulation by PMA and cGMP caused at least a 100% increase in mucus secretion over control levels. This increased was however blocked by pre- and co-incubation with

the **MANS peptide**. Levels of secreted mucus fell to control values when 10 muM **peptide** was used, and levels of secreted mucus were well below control values following incubation with 100 muM **MANS peptide**. The **MANS peptide** was also found to decrease constitutive basal mucus secretion by 1 hour incubation.

=> d all abeq tech abex

L66 ANSWER 1 OF 1 WPIX (C) 2003 THOMSON DERWENT
AN **2003-221725** [21] WPIX
DNC **C2003-056492**
TI Preventing or delaying programmed cell death in a recombinant cell comprises expressing one or more anti-apoptotic polypeptide(s) in the cell such that programmed cell death in the cell is prevented or delayed.
DC B04 D16
IN AILOR, E; BETENBAUGH, M J; FIGUEROA, B; HARDWICK, M; REFF, M E; REFF, M
PA (IDEC-N) IDEC PHARM CORP
CYC 100
PI WO 2003006607 A2 20030123 (200321)* EN 41p C12N000-00
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
US 2003064510 A1 20030403 (200325) A61K038-19 <--
ADT WO 2003006607 A2 WO 2002-US21606 20020710; US 2003064510 A1 Provisional US 2001-303813P 20010710, US 2002-191052 20020710
PRAI US 2001-303813P 20010710; US 2002-191052 20020710
IC ICM **A61K038-19**; C12N000-00
ICS **A61K038-43**; **A61K039-395**; C12N005-06; C12P021-02
AB WO2003006607 A UPAB: 20030328
NOVELTY - Preventing or delaying programmed cell death in a recombinant cell that is not a mouse myeloma cell, comprises expressing one or more anti-apoptotic polypeptide(s) in the cell such that programmed cell death in the cell is prevented or delayed. The anti-apoptotic polypeptide is not Aven.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) methods of increasing production of a recombinant cell or a cell-related product by a recombinant cell, comprising expressing one or more anti-apoptotic polypeptide(s) in the cell such that production of the recombinant cell, or the cell-related product by the cell, is increased; and

(2) a recombinant cell, or a population of cells, useful for producing a cell-related product expressing or is capable of expressing at least 2 anti-apoptotic polypeptides.

ACTIVITY - None given.

MECHANISM OF ACTION - Anti-apoptotic.

Expression of E1B-19K alone and Aven alone has an anti-apoptotic, viability increasing effect (cell viability 60% after 2 days culture), and the effect of E1B-19K alone is very significant and greater than Aven alone and the expression of the 2 genes in combination yields a synergistic effect (cell viability 80% after 2 days culture).

USE - The method is useful in inhibiting apoptotic process and in improving cell performance. The recombinant cells are used for cellular therapy and in producing a cell-related product.

Dwg.0/37
FS CPI
FA AB; DCN

MC CPI: B04-F0200E; B04-G0100E; B04-H0100E; B04-K0100E; B04-L0100E;
B04-N0400E; B14-S03; D05-H14; D05-H14B2; D05-H17A
TECH UPTX: 20030328
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: In preventing or delaying programmed cell death in a recombinant cell, the cell comprises one or more heterologous polynucleotides encoding one or more desired polypeptide(s). The desired polypeptides are selected from antibodies, enzymes, receptors, cytokines, cell-surface factors, cell metabolites, cell-secretion factors, viral factors and **membrane-associated factors**. The antibodies are selected from anti-CD154 antibodies (IEC-131), anti-CD20 antibodies (Rituxan (RTM) or Zevalin (RTM)), anti-B7 antibodies (IDEC114), anti-CD23 antibodies (IDEC152), anti-CD4 antibodies (IDEC151), and anti-tumor antigen antibodies. The expression of the apoptotic polypeptides is controlled by at least one inducible heterologous promoter operably linked to the above polynucleotide encoding the anti-apoptotic polypeptides. The inducible heterologous promoter is an ecdysone promoter that is inducible by a steroid. The recombinant cell further comprises a screenable or selectable marker operably linked to the inducible heterologous promoter. The marker is a green fluorescence protein (GFP) or an enhanced green fluorescence protein (EGF). The anti-apoptotic polypeptide is encoded by genes in eukaryotic cells or viruses, and is selected from Bcl-xL, Bcl-2, Aven, E1B-19K, and p35. The method comprises expressing one apoptotic polypeptide such as E1B-19K, or expressing at least 2 polypeptides such as E1B-19K and Aven. The recombinant cell is a mammalian cell, such as a human cell, murine cell or rodent cell. The recombinant cell is a CHO cell or a BHK cell. The CHO cell is a CHO 5C11. It is in a large-scale bioreactor or culture device of a commercial production. In increasing the production of a cell-related product by a recombinant cell, the cell-related product is a recombinant protein, antibody, enzyme, receptor, cytokine, cell-surface factor, cell metabolite, cell-secretion factor, viral factor, **membrane-associated factor**, or a polynucleotide.

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FILE LAST UPDATED: 9 May 2003 (20030509/ED)

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L138 ANSWER 1 OF 12 HCAPLUS COPYRIGHT 2003 ACS
AN **2001:400604** HCAPLUS

DN **135:135832**
TI Amyloid .beta. **protein** activates PKC-.delta. and induces translocation of **myristoylated alanine-rich C kinase substrate** (**MARCKS**) in microglia
AU Nakai, Masamichi; Tanimukai, Satoshi; Yagi, Keiko; Saito, Naoaki; Taniguchi, Taizo; Terashima, Akira; Kawamata, Toshio; Yamamoto, Hideyuki; Fukunaga, Kohji; Miyamoto, Eishichi; Tanaka, Chikako
CS Hyogo Institute for Aging Brain and Cognitive Disorders, Himeji, 670-0981, Japan
SO Neurochemistry International (**2001**), 38(7), 593-600
CODEN: NEUIDS; ISSN: 0197-0186
PB Elsevier Science Ltd.
DT Journal
LA English
CC 14-10 (Mammalian **Pathological** Biochemistry)
AB The increased accumulation of activated microglia contg. amyloid .beta. **protein** (A.beta.) around senile plaques is a common pathol. feature in subjects with Alzheimer's disease (AD). Much less is known, however, of intracellular signal transduction pathways for microglial activation in response to A.beta.. We investigated intracellular signaling in response to A.beta. stimulation in primary cultured rat microglia. We found that the kinase activity of PKC-.delta. but not that of PKC-.alpha. or -.epsilon. is increased by stimulation of microglia with A.beta., with a striking tyrosine phosphorylation of PKC-.delta.. In microglia stimulated with A.beta., tyrosine phosphorylation of PKC-.delta. was evident at the membrane fraction without an overt translocation of PKC-.delta.. PKC-.delta. co-immuno-pptd. with **MARCKS** from microglia stimulated with A.beta.. A.beta. induced translocation of **MARCKS** from the membrane fraction to the cytosolic fraction. Immunocytochem. anal. revealed that phosphorylated **MARCKS** accumulated in the cytoplasm, particularly at the perinuclear region in microglia treated with A.beta.. Taken together with our previous observations that A.beta.-induced phosphorylation of **MARCKS** and chemotaxis of microglia are inhibited by either tyrosine kinase or PKC inhibitors, our results provide evidence that A.beta. induces phosphorylation and translocation of **MARCKS** through the tyrosine kinase-PKC-.delta. signaling pathway in microglia.
ST Alzheimer amyloid **protein** kinase C **MARCKS** microglia
IT Alzheimer's disease
(amyloid .beta. **protein** activates PKC-.delta. and induces translocation of **myristoylated alanine-rich C kinase substrate** (**MARCKS**) in microglia)
IT **MARCKS** (**myristoylated alanine-rich C kinase substrate**)
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(amyloid .beta. **protein** activates PKC-.delta. and induces translocation of **myristoylated alanine-rich C kinase substrate** (**MARCKS**) in microglia)
IT **Biological transport**
(intracellular; amyloid .beta. **protein** activates PKC-.delta. and induces translocation of **myristoylated alanine-rich C kinase substrate** (**MARCKS**) in microglia)
IT Neuroglia
(microglia; amyloid .beta. **protein** activates PKC-.delta. and induces translocation of **myristoylated alanine-rich C kinase substrate** (**MARCKS**) in microglia)
IT Phosphorylation, biological

(**protein**; amyloid .beta. **protein** activates PKC-.delta. and induces translocation of **myristoylated alanine-rich C kinase substrate** (**MARCKS**) in microglia)

IT 131438-79-4 131602-53-4
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(amyloid .beta. **protein** activates PKC-.delta. and induces translocation of **myristoylated alanine-rich C kinase substrate** (**MARCKS**) in microglia)

IT 141436-78-4, **Protein** kinase C
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(.delta.; amyloid .beta. **protein** activates PKC-.delta. and induces translocation of **myristoylated alanine-rich C kinase substrate** (**MARCKS**) in microglia)

RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE
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L138 ANSWER 2 OF 12 HCAPLUS COPYRIGHT 2003 ACS
AN **2000:775411** HCAPLUS
DN **134:15966**
TI Endotoxin causes phosphorylation of **MARCKS** in pulmonary vascular endothelial cells
AU Zhao, Ying; Davis, Harold W.
CS Department of Internal Medicine (Pulmonary/Critical Care Medicine), University of Cincinnati Medical Center, Cincinnati, OH, 45267-0564, USA
SO Journal of Cellular Biochemistry (**2000**), 79(3), 496-505
CODEN: JCEBD5; ISSN: 0730-2312
PB Wiley-Liss, Inc.
DT Journal

LA English
CC 14-3 (Mammalian **Pathological** Biochemistry)
AB **Protein** kinase C (PKC) has been implicated in lipopolysaccharide (LPS)-induced endothelial cell (EC) monolayer permeability. **Myristoylated alanine-rich C kinase substrate** (**MARCKS**), as a specific PKC substrate, appears to mediate PKC signaling by PKC-dependent phosphorylation of **MARCKS** and subsequent modification of the assocn. of **MARCKS** with filamentous actin and calmodulin (CaM). Therefore, in the present study, we investigated LPS-induced **MARCKS** phosphorylation in bovine pulmonary artery EC (BPAEC). LPS potentiated **MARCKS** phosphorylation in BPAEC in a time- and dose-dependent manner. The PKC inhibitor, calphostin C, significantly decreased LPS-induced phosphorylation of **MARCKS**. In addn., downregulation of PKC with phorbol 12-myristate 13-acetate (PMA) did not affect the LPS-induced **MARCKS** phosphorylation, suggesting that LPS and PMA activate different isoforms of PKC. Pretreatment with SB203580, a specific inhibitor of p38 MAP kinase, or genistein, a tyrosine kinase inhibitor, prevented LPS-induced **MARCKS** phosphorylation. Phosphorylation at appropriate sites will induce translocation of **MARCKS** from the cell membrane to the cytosol. However, LPS, in contrast to PMA, did not generate **MARCKS** translocation in BPAEC, suggesting that **MARCKS** translocation may not play a role in LPS-induced actin rearrangement and EC permeability. LPS also enhanced both thrombin- and PMA-induced phosphorylation of **MARCKS**, suggesting that LPS was able to prime these signaling pathways in BPAEC. Because the CaM-dependent phosphorylation of myosin light chains (MLC) results in EC contraction, we studied the effect of LPS on MLC phosphorylation in BPAEC. LPS induced dephosphorylation of MLC in a time-dependent manner, which occurred at lower doses of LPS, than those required to induce **MARCKS** phosphorylation. In addn., there was no synergism between LPS and thrombin in the induction of MLC phosphorylation. These data indicate that MLC phosphorylation is independent of **MARCKS** phosphorylation. In conclusion, LPS stimulated **MARCKS** phosphorylation in BPAEC. This phosphorylation appears to involve activation of PKC, p38 MAP kinase, and tyrosine kinases. Further studies are needed to explore the role of **MARCKS** phosphorylation in LPS-induced actin rearrangement and EC permeability.
ST lipopolysaccharide **protein** kinase **MARCKS** phosphorylation pulmonary artery endothelium sepsis; p38 MAPK tyrosine kinase **MARCKS** phosphorylation vascular permeability
IT Lipopolysaccharides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(bacterial; p38 MAP kinase and tyrosine kinase in endotoxin-induced **protein** kinase C-dependent phosphorylation of **MARCKS** in pulmonary vascular endothelial cells)
IT **Myosins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(light-chain; p38 MAP kinase and tyrosine kinase in endotoxin-induced **protein** kinase C-dependent phosphorylation of **MARCKS** in pulmonary vascular endothelial cells in relation to)
IT **MARCKS (myristoylated alanine-rich C kinase substrate)**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(p38 MAP kinase and tyrosine kinase in endotoxin-induced **protein** kinase C-dependent phosphorylation of **MARCKS** in pulmonary vascular endothelial cells)
IT Sepsis
(p38 MAP kinase and tyrosine kinase in endotoxin-induced

protein kinase C-dependent phosphorylation of **MARCKS** in pulmonary vascular endothelial cells in relation to)

IT Blood vessel
(permeability; p38 MAP kinase and tyrosine kinase in endotoxin-induced **protein** kinase C-dependent phosphorylation of **MARCKS** in pulmonary vascular endothelial cells)

IT **Biological transport**
(permeation, vascular; p38 MAP kinase and tyrosine kinase in endotoxin-induced **protein** kinase C-dependent phosphorylation of **MARCKS** in pulmonary vascular endothelial cells)

IT Phosphorylation, biological
(**protein**; p38 MAP kinase and tyrosine kinase in endotoxin-induced **protein** kinase C-dependent phosphorylation of **MARCKS** in pulmonary vascular endothelial cells)

IT Artery
(pulmonary, endothelium; p38 MAP kinase and tyrosine kinase in endotoxin-induced **protein** kinase C-dependent phosphorylation of **MARCKS** in pulmonary vascular endothelial cells)

IT 80449-02-1, Tyrosine kinase 141436-78-4, **Protein** kinase C
165245-96-5, P38 MAP kinase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(p38 MAP kinase and tyrosine kinase in endotoxin-induced **protein** kinase C-dependent phosphorylation of **MARCKS** in pulmonary vascular endothelial cells)

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L138 ANSWER 3 OF 12 HCAPLUS COPYRIGHT 2003 ACS
AN **2000:472316** HCAPLUS
DN **133:190866**
TI Macrophage-enriched **myristoylated alanine-rich C kinase substrate** and its phosphorylation is required for the phorbol ester-stimulated diffusion of .beta.2 integrin molecules
AU Zhou, Ximing; Li, Jianxun
CS Department of Oral Biology, College of Dentistry, University of Illinois, Chicago, IL, 60612, USA
SO Journal of Biological Chemistry (**2000**), 275(26), 20217-20222
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
CC 13-2 (Mammalian Biochemistry)
Section cross-reference(s): **15**
AB An early event of .beta.2 integrin activation is the increased diffusion rate of this mol. on the cell surface, thereby providing integrin mols. with a better chance to meet the ligands. The activation of **protein** kinase C (PKC) stimulates integrin diffusion by releasing the cytoskeletal constraint on integrin mols. We report here that macrophage-enriched **myristoylated alanine-rich C kinase substrate** (**MacMARCKS**), a membrane-assocd. PKC substrate involved in integrin activation, is required for this PKC-stimulated diffusion of integrin mols. Using the single-particle tracking technique, we obsd. that the activation of PKC stimulated an 11-fold increase in the diffusion rate of .beta.2 integrins in wild type J774 macrophage cells but not in those expressing mutant **MacMARCKS**. Further evidence is provided from a **MacMARCKS** -deficient cell line in which phorbol esters failed to stimulate the diffusion of integrin. Transfection of wild type **MacMARCKS** into these cells restored the rapid diffusion rate of the .beta.2 integrins. The phosphorylation of **MacMARCKS** is important because transfection of a non-phosphorylatable **MacMARCKS** mutant or the addn. of staurosporine eliminates the rapid diffusion rate of integrin. Furthermore, adding cytochalasin D bypasses the **MacMARCKS** deficiency and stimulates .beta.2 integrin diffusion, suggesting that **MacMARCKS**'s involvement in integrin activation is prior or at the site of cytoskeleton. Therefore, we conclude that **MacMARCKS** is required for releasing the cytoskeletal constraint on integrin mols. during PKC-mediated integrin activation.
ST **MARCKS** phosphorylation **protein** kinase integrin diffusion cytoskeleton macrophage
IT **Biological transport**
(diffusion; macrophage-enriched **myristoylated alanine -rich C kinase substrate** and its phosphorylation in **protein** kinase C-stimulated diffusion of .beta.2 integrin mols.)
IT Cytoskeleton
Macrophage
(macrophage-enriched **myristoylated alanine-rich C kinase substrate** and its phosphorylation in **protein** kinase C-stimulated diffusion of .beta.2 integrin mols.)
IT **MARCKS** (**myristoylated alanine-rich C kinase substrate**)
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(macrophage-enriched **myristoylated alanine-rich C kinase substrate** and its phosphorylation in **protein** kinase C-stimulated diffusion of

.beta.2 integrin mols.)
IT Phosphorylation, biological
(**protein**; macrophage-enriched **myristoylated alanine-rich C kinase substrate** and its phosphorylation in **protein** kinase C-stimulated diffusion of .beta.2 integrin mols.)
IT Integrins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(.beta.2; macrophage-enriched **myristoylated alanine-rich C kinase substrate** and its phosphorylation in **protein** kinase C-stimulated diffusion of .beta.2 integrin mols.)
IT 141436-78-4, **Protein** kinase C
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(macrophage-enriched **myristoylated alanine-rich C kinase substrate** and its phosphorylation in **protein** kinase C-stimulated diffusion of .beta.2 integrin mols.)
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L138 ANSWER 4 OF 12 HCAPLUS COPYRIGHT 2003 ACS
AN **1999:476384** HCAPLUS
DN **131:241938**
TI Phagocytic and macropinocytic activity in **MARCKS**-deficient macrophages and fibroblasts
AU Carballo, Ester; Pitterle, Diana M.; Stumpo, Deborah J.; Sperling, Robert T.; Blackshear, Perry J.
CS Office of Clinical Research and Laboratory of Signal Transduction, National Institute of Environmental Health Sciences, Research Triangle Park, NC, 27709, USA
SO American Journal of Physiology (**1999**), 277(1, Pt. 1), C163-C173
CODEN: AJPHAP; ISSN: 0002-9513
PB American Physiological Society
DT Journal
LA English
CC **15-10** (Immunochemistry)
AB Macrophages express high levels of the **myristoylated, alanine-rich, C kinase substrate** (**MARCKS**), an actin crosslinking **protein**. To investigate a possible role of **MARCKS** in macrophage function, fetal liver-derived macrophages were generated from wild-type and **MARCKS** knockout mouse embryos. No differences between the wild-type and **MARCKS**-deficient macrophages with respect to morphol. (Wright's stain) or actin distribution (staining with rhodamine-phalloidin, under basal conditions or after treatment with phorbol esters, lipopolysaccharide, or both) were obsd. We then evaluated phagocytosis mediated by different receptors: Fc receptors tested with IgG-coated sheep red blood cells, complement C3b receptors tested with C3b-coated yeast, mannose receptors tested with unopsonized zymosan, and nonspecific phagocytosis tested with latex beads. We also studied fluid phase endocytosis in macrophages and mouse embryo fibroblasts by using FITC-dextran to quantitate this process. In most cases, there were no differences between the cells derived from wild-type and **MARCKS** -deficient mice. However, a minor but significant and reproducible difference in rates of zymosan phagocytosis at 45-60 min was obsd., with lower rates of phagocytosis in the **MARCKS**-deficient cells. Our data indicate that **MARCKS** deficiency may lead to slightly decreased rates of zymosan phagocytosis.
ST macrophage phagocytosis **MARCKS** zymosan
IT **Pinocytosis**
(macropinocytosis; phagocytic and macropinocytic activity in **MARCKS**-deficient macrophages and fibroblasts)
IT Fibroblast
Macrophage
Phagocytosis
(phagocytic and macropinocytic activity in **MARCKS**-deficient macrophages and fibroblasts)
IT **MARCKS (myristoylated alanine-rich C kinase substrate)**
Zymosans
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(phagocytic and macropinocytic activity in **MARCKS**-deficient macrophages and fibroblasts)
RE.CNT 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD
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L138 ANSWER 5 OF 12 HCAPLUS COPYRIGHT 2003 ACS
AN **1999:206120** HCAPLUS
DN **131:3669**

TI Mechanisms involved in the contraction of endothelial cells by hydrogen peroxide

AU Lopez-Ongil, Susana; Torrecillas, Guadalupe; Perez-Sala, Dolores; Gonzalez-Santiago, Laura; Rodriguez-Puyol, Manuel; Rodriguez-Puyol, Diego

CS Department of Physiology and Pharmacology, Alcala de Henares University, Madrid, Spain

SO Free Radical Biology & Medicine (**1999**), 26(5/6), 501-510
CODEN: FRBMEH; ISSN: 0891-5849

PB Elsevier Science Inc.

DT Journal

LA English

CC 14-5 (Mammalian **Pathological** Biochemistry)

AB The importance of endothelial contraction in the genesis of inflammatory edema has been reported. ROS are metabolites synthesized in pathol. conditions in that a significant intravascular fluid leak occurs, such as ischemia-reperfusion. Present expts. were designed to test the hypothesis that ROS, particularly H2O2, may elicit the contraction of endothelial cells, and to explore the mechanisms involved. Bovine aortic endothelial cells incubated with H2O2 showed a significant redn. in planar cell surface area (PCSA), and a significant increase in myosin light chain phosphorylation (MLCP), with a time- and dose-dependent pattern, without any significant toxicity. This effect of H2O2 was not blocked by sulotroban (TxA2 antagonist) or BN 52021 (PAF antagonist). Lanthanum chloride (calcium channel blocker) and EGTA partially inhibited the increase in MLCP induced by H2O2. H7 and staurosporine, PKC inhibitors, and PKC down-regulation (phorbol myristate acetate treatment, 24 h) also blocked H2O2-dependent endothelial contraction, measured as PCSA or MLCP. H2O2 increased the intracellular calcium concn., an effect blunted by EGTA and lanthanum chloride. H2O2 also increased the phosphorylation of an 80 kDa **polypeptide**, probably **MARCKS**, a PKC substrate. In summary, the present results demonstrate the ROS-dependent contraction of endothelial cells, an effect that could explain the intravascular fluid leak obsd. in some pathophysiol. situations. Calcium and PKC may be involved in the development of this contraction.

ST endothelium contraction hydrogen peroxide edema

IT Artery
(aorta, endothelium; mechanisms involved in contraction of endothelial cells by hydrogen peroxide)

IT Blood vessel
(endothelium; mechanisms involved in contraction of endothelial cells by hydrogen peroxide)

IT **Inflammation**
Inflammation
(**inflammatory edema**; mechanisms involved in contraction of endothelial cells by hydrogen peroxide)

IT Edema
Edema
(inflammatory; mechanisms involved in contraction of endothelial cells by hydrogen peroxide)

IT **Myosins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(light chains of, phosphorylation; mechanisms involved in contraction of endothelial cells by hydrogen peroxide)

IT Reactive oxygen species
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(mechanisms involved in contraction of endothelial cells by hydrogen peroxide)

IT **MARCKS (myristoylated alanine-rich C kinase substrate)**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(phosphorylation of; mechanisms involved in contraction of endothelial

cells by hydrogen peroxide)
IT Phosphorylation, biological
(**protein**, of MARKS and myosin light chains; mechanisms involved in contraction of endothelial cells by hydrogen peroxide)
IT 7722-84-1, Hydrogen peroxide, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(mechanisms involved in contraction of endothelial cells by hydrogen peroxide)
IT 141436-78-4, **Protein** kinase C
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(mechanisms involved in contraction of endothelial cells by hydrogen peroxide)
IT 7440-70-2, Calcium, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(mechanisms involved in contraction of endothelial cells by hydrogen peroxide)
IT 7782-44-7, Oxygen, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(reactive species; mechanisms involved in contraction of endothelial cells by hydrogen peroxide)
RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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L138 ANSWER 6 OF 12 HCAPLUS COPYRIGHT 2003 ACS
AN **1999:117** HCAPLUS
DN **130:167026**
TI **MacMARCKS** is not essential for phagocytosis in macrophages
AU Underhill, David M.; Chen, Jianmin; Allen, Lee-Ann H.; Aderem, Alan
CS Department of Immunology, University of Washington, Seattle, WA, 98195, USA
SO Journal of Biological Chemistry (**1998**), 273(50), 33619-33623
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
CC **15-6** (Immunochemistry)
AB **MacMARCKS** (also known as myristoylated alanine-rich **protein** kinase C substrate (**MARCKS**)-related **protein**) is a member of the **MARCKS** family of **protein** kinase C substrates. **MacMARCKS** contains within it a basic effector domain that contains the serine residues that are phosphorylated by **protein** kinase C, as well as a calcium/calmodulin and actin-binding site. Two previous reports demonstrated that a macrophage cell line expressing a mutant form of **MacMARCKS** that lacks the effector domain is defective in phagocytosis and cell adhesion. The authors report here that macrophages from **MacMARCKS** null mice phagocytose and spread normally. Thus, although **MacMARCKS** is recruited to phagosomes, it is not absolutely required for phagocytosis.
ST **MacMARCKS** phagocytosis macrophage
IT Phospholipoproteins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**MacMARCKS**; **MacMARCKS** is not essential for phagocytosis in macrophages)
IT Leukocyte
(adhesion; **MacMARCKS** is not essential for phagocytosis in macrophages in relation to)
IT Spreading
(biol.; **MacMARCKS** is not essential for phagocytosis in macrophages in relation to)
IT Cell adhesion
(leukocyte; **MacMARCKS** is not essential for phagocytosis in macrophages in relation to)
IT **Phagocytosis**
(macrophage; **MacMARCKS** is not essential for)
IT Macrophage
(phagocytosis; **MacMARCKS** is not essential for)
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
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(2) Allen, L; EMBO J 1995, V14, P1109 HCAPLUS
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L138 ANSWER 7 OF 12 HCAPLUS COPYRIGHT 2003 ACS
AN **1998:223709** HCAPLUS
DN **129:3378**
TI Overexpression of the **myristoylated alanine-rich C kinase substrate** in human choroidal melanoma cells affects cell proliferation
AU Manenti, Stephane; Malecaze, Francois; Chap, Hugues; Darbon, Jean-Marie
CS Institut National de la Sante et de la Recherche Medicale (INSERM), Institut Federatif de Recherche 30, Toulouse, 31059, Fr.
SO Cancer Research (**1998**), 58(7), 1429-1434
CODEN: CNREA8; ISSN: 0008-5472
PB American Association for Cancer Research
DT Journal
LA English
CC 14-1 (Mammalian **Pathological** Biochemistry)
AB Reduced expression of the **myristoylated alanine-rich C kinase substrate** (**MARCKS**) has been described in various cell lines after oncogenic or chem. transformation, leading to the question of whether this **protein** may be involved in cell proliferation. Here we compare the expression of **MARCKS** in human tumor-derived choroidal melanoma cells (OCM-1) and in primary cultures of normal choroidal melanocytes. We found an important down-regulation of the **protein** in the melanoma cell line. Stable transfection of these cells with the cDNA coding for **MARCKS** led to the selection of several clones expressing variable levels of the **protein**. Proliferation expts. performed with four of these clones revealed that cell growth was reduced by 35-40% when compared with control cells. Upon serum starvation, cell proliferation was almost abolished when the expression level of **MARCKS** was high, whereas it was only partially reduced in the controls. **MARCKS** overexpression induced a higher percentage of cells in the G0-G1 phase of the cell cycle upon serum starvation, as well as the inhibition of colony formation in soft agar. Finally, the expression of the CDK inhibitor p27 was increased in the cells presenting a high level of **MARCKS protein**. Altogether, these data suggest that the expression of this **protein** kinase C substrate affects the proliferation and partially reverts the transformed phenotype of the OCM-1 cells.
ST **MARCKS** cell proliferation eye melanoma
IT Eye
(choroid, melanoma; overexpression of **myristoylated alanine-rich C kinase substrate** in human choroidal melanoma cells affects cell proliferation)
IT Eye, neoplasm
Eye, neoplasm
(melanoma; overexpression of **myristoylated alanine-rich C kinase substrate** in human choroidal melanoma cells affects cell proliferation)

IT Cell cycle
Cell proliferation
Melanocyte
(overexpression of **myristoylated alanine-rich C kinase substrate** in human choroidal melanoma cells affects cell proliferation)
IT **MARCKS (myristoylated alanine-rich C kinase substrate)**
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(overexpression of **myristoylated alanine-rich C kinase substrate** in human choroidal melanoma cells affects cell proliferation)
IT Cyclin dependent kinase inhibitors
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(p27KIP1; overexpression of **myristoylated alanine-rich C kinase substrate** in human choroidal melanoma cells affects cell proliferation)
RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
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L138 ANSWER 8 OF 12 HCAPLUS COPYRIGHT 2003 ACS
AN **1996:274324** HCAPLUS
DN **124:339516**
TI **MARCKS** functions as a novel growth suppressor in cells of melanocyte origin
AU Brooks, Gavin; Brooks, Susan F.; Goss, Martin W.
CS Eisai London Research Laboratories, University College, London, UK
SO Carcinogenesis (**1996**), 17(4), 683-689
CODEN: CRNGDP; ISSN: 0143-3334
PB Oxford University Press
DT Journal
LA English
CC 14-1 (Mammalian **Pathological** Biochemistry)
Section cross-reference(s): 3
AB **Protein** kinase C (PKC) plays a pivotal role in modulating the growth of melanocytic cells in culture. We have shown previously that a major physiol. substrate of PKC, the 80 kDa **myristoylated alanine-rich C-kinase substrate** (**MARCKS**), can be phosphorylated in quiescent, non-tumorigenic melanocytes exposed transiently to a biol. active phorbol ester, but cannot be phosphorylated in phorbol ester-treated, syngeneic malignant melanoma cells. Despite its ubiquitous distribution, the function of **MARCKS** in cell growth and transformation remains to be demonstrated clearly. We report here that **MARCKS** mRNA and **protein** levels are down-regulated significantly in the spontaneously derived murine B16 melanoma cell line compared with syngeneic normal Mel-ab melanocytes. In contrast, the tumorigenic v-Ha-ras-transformed melanocytic line, LTR Ras 2, showed a high basal level of **MARCKS** phosphorylation which was not enhanced by treatment of cells with phorbol ester. Furthermore, **protein** levels of **MARCKS** in LTR Ras 2 cells were similar to those expressed in Mel-ab melanocytes. However, in four out of six murine tumor cell lines investigated, levels of **MARCKS protein** were barely detectable. Transfection of B16 cells with a plasmid contg. the **MARCKS** cDNA in the sense orientation produced two neomycin-resistant clones displaying reduced proliferative capacity and decreased anchorage-independent growth compared with control cells. In contrast, transfection with the antisense **MARCKS** construct produced many colonies which displayed enhanced growth and transforming potential compared with control cells. Thus, **MARCKS** appears to act as a novel growth suppressor in the spontaneous transformation of cells of melanocyte origin and may play a more general role in the tumor progression of other carcinomas.
ST melanocyte transformation melanoma **protein MARCKS**
IT Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**MARCKS**; **protein MARCKS** expression in spontaneous transformation of melanocytic cells and B16 melanoma cell proliferation)
IT Cell proliferation
Melanocyte
Melanoma
Phosphorylation, biological
Transcription, genetic
Transformation, neoplastic
(**protein MARCKS** expression in spontaneous transformation of melanocytic cells and B16 melanoma cell proliferation)
IT Phospholipoproteins
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(**MARCKS** (**myristoylated alanine-rich C kinase substrate**), **protein MARCKS** expression in spontaneous transformation of melanocytic cells and B16 melanoma cell proliferation)

IT 141436-78-4, **Protein** kinase C
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**protein MARCKS** expression in spontaneous transformation of melanocytic cells and B16 melanoma cell proliferation)

L138 ANSWER 9 OF 12 HCAPLUS COPYRIGHT 2003 ACS
AN **1995:760102** HCAPLUS
DN **123:167374**
TI A role for **MARCKS**, the .alpha. isozyme of **protein** kinase C and myosin I in zymosan phagocytosis by macrophages
AU Allen, Lee-Ann H.; Aderem, Alan
CS Laboratory Signal Transduction, Rockefeller Univ., New York, NY, 10021, USA
SO Journal of Experimental Medicine (**1995**), 182(3), 829-40
CODEN: JEMEAV; ISSN: 0022-1007
PB Rockefeller University Press
DT Journal
LA English
CC **15-6** (Immunochemistry)
AB **Myristoylated, alanine-rich C-kinase substrate** (**MARCKS**) is a lipopolysaccharide-induced **protein** kinase C (PKC) substrate that has been proposed to regulate actin-membrane interactions, as well as actin structure at the membrane. The authors studied the distribution of **MARCKS**, the .alpha. isozyme of PKC (PKC.alpha.), and myosin I in lipopolysaccharide-treated peritoneal macrophages ingesting zymosan particles. **MARCKS**, PKC.alpha., and myosin I colocalized with F-actin and talin in the cortical cytoplasm adjacent to forming phagocytic cups. After particle ingestion was completed, myosin I, F-actin, and talin were no longer enriched in the vicinity of the phagosome. By contrast, **MARCKS** and PKC.alpha. remained assocd. with the phagosome membrane until after acquisition of the lysosomal marker Lamp-1. Vinculin was not detected on phagosomes at any time point examd. Phagocytosis of zymosan was accompanied by rapid and sustained phosphorylation of **MARCKS**. Inhibitors of PKC reduced zymosan binding to the macrophage surface and blocked the focal accumulation of F-actin, talin, phosphotyrosine-contg. **proteins, MARCKS**, and PKC.alpha. beneath attached particles. The authors propose that PKC-dependent phosphorylation is an early signal required for zymosan phagocytosis and that **MARCKS** and PKC.alpha. have a role in phagosome maturation. The colocalization of F-actin and **MARCKS** at the cytoplasmic face of the nascent phagosome reinforces the hypothesis that **MARCKS** regulates actin structure at the membrane. The data also suggest that myosin I functions as a mech. motor during particle uptake.
ST **MARCKS protein** kinase C phagocytosis macrophage; myosin I zymosan phagocytosis macrophage
IT Macrophage
Phagocytosis
(**MARCKS, protein** kinase C .alpha. isozyme, and myosin I in zymosan phagocytosis by macrophages)
IT Zymosans
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**MARCKS, protein** kinase C .alpha. isozyme, and myosin I in zymosan phagocytosis by macrophages)

IT Phosphorylation, biological
Signal transduction, biological
(**protein** kinase C-dependent phosphorylation is early signal required for zymosan phagocytosis by macrophage)
IT **Myosins**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(I, **MARCKS, protein** kinase C .**alpha.** isozyme, and myosin I in zymosan phagocytosis by macrophages)
IT Phospholipoproteins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**MARCKS (myristoylated alanine-rich C kinase substrate)**, **MARCKS, protein** kinase C .alpha. isozyme, and myosin I in zymosan phagocytosis by macrophages)
IT 141436-78-4, **Protein** kinase C
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(.alpha.; **MARCKS, protein** kinase C .alpha. isozyme, and myosin I in zymosan phagocytosis by macrophages)

L138 ANSWER 10 OF 12 HCAPLUS COPYRIGHT 2003 ACS
AN **1995:386940** HCAPLUS
DN **122:157379**
TI The role of 80K/**MARCKS**, a specific substrate of **protein** kinase C, in cell growth and tumor progression
AU Brooks, Gavin
CS Rayne Institute, St. Thomas' Hospital, London, SE1 7EH, UK
SO Pigment Cell Research (**1994**), 7(6), 451-7
CODEN: PCREEA; ISSN: 0893-5785
DT Journal; General Review
LA English
CC 14-0 (Mammalian **Pathological** Biochemistry)
Section cross-reference(s): 13
AB A review, with 50 refs. Since its discovery more than a decade ago, the 80-87 kDa **myristoylated alanine-rich C-kinase substrate** (80K/**MARCKS**) **protein** has attracted a great deal of attention from researchers interested in cell growth and tumor progression. However, despite its ubiquitous distribution, a definitive functional role for 80K/**MARCKS** has not been found. The purpose of this review is to describe the properties, distribution and regulation of 80K/**MARCKS** and to discuss some of the most recent findings, both from our lab. and from others, that have suggested a functional role for this **protein** in modulating cell growth and tumor progression. Furthermore, the author will presents data from his lab. that implicates 80K/**MARCKS** as a novel tumor suppressor in cells of melanocyte origin.
ST review melanocyte melanoma **protein** MARKS
IT **Melanocyte**
Melanoma
(**protein MARCKS** in melanocyte cell growth and melanoma in human and lab. animals)
IT Phospholipoproteins
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(**MARCKS (myristoylated alanine-rich C kinase substrate)**, **protein MARCKS** in melanocyte cell growth and melanoma

in human and lab. animals)

L138 ANSWER 11 OF 12 HCAPLUS COPYRIGHT 2003 ACS
AN **1993:445848** HCAPLUS
DN **119:45848**
TI The **MARCKS protein**: A PKC substrate which regulates cytoskeletal-membrane interactions
AU Aderem, Alan; Seykora, John T.
CS Lab. Signal Transduct., Rockefeller Univ., New York, NY, 10021, USA
SO Protein Kinase C (**1992**), 255-73. Editor(s): Lester, David S.; Epand, Richard M. Publisher: Horwood, Chichester, UK.
CODEN: 59BLAU
DT Conference; General Review
LA English
CC 13-0 (Mammalian Biochemistry)
Section cross-reference(s): 7, **15**
AB A review with 68 refs. on the properties of **MARCKS** and the evidence which supports the model proteinase C (PKC)-mediated phosphorylation-dependent manner. Because the translocation phenomena of the **MARCKS protein** has been extensively characterized in murine macrophages and human neutrophils, the behavior of **MARCKS** in these systems is emphasized.
ST review **MARCKS** phosphorylation cytoskeleton membrane translocation; kinase C **MARCKS protein** regulation review; macrophage **MARCKS** regulation review; neutrophil **MARCKS** regulation review
IT Phosphorylation, biological
(MARKS **protein** cytoplasmic-membrane interactions regulation by)
IT Cell membrane
Cytoskeleton
(MARKS **protein** interaction with and localization in, phosphorylation dependence of)
IT Macrophage
Neutrophil
(MARKS **protein** of, phosphorylation-dependent regulation and properties of)
IT Phospholipoproteins
RL: BIOL (Biological study)
(**MARCKS (myristoylated alanine-rich C kinase substrate)**, phosphorylation-dependent regulation and properties of, cytoskeleton-membrane translocation in relation to)
IT **Biological transport**
(translocation, of **MARCKS protein**, between cell membrane and cytoskeleton, phosphorylation in regulation of)
IT 141436-78-4, **Protein** kinase C
RL: BIOL (Biological study)
(MARKS **protein** cytoskeleton-membrane translocation regulation by)

L138 ANSWER 12 OF 12 HCAPLUS COPYRIGHT 2003 ACS
AN **1992:585567** HCAPLUS
DN **117:185567**
TI **Membrane-associated neurotransmitter stimulating factor** is very similar to ciliary neurotrophic **factor**
AU Rao, M.; Patterson, P. H.; Landis, S. C.
CS Dep. Neurosci., Case West. Reserve Univ., Cleveland, OH, 44106, USA
SO Developmental Biology (Orlando, FL, United States) (**1992**), 153(2), 411-16
CODEN: DEBIAO; ISSN: 0012-1606
DT Journal

LA English
CC 2-10 (Mammalian Hormones)
AB **Membrane-assocd. neurotransmitter stimulating factor** (**MANS**) can modulate sympathetic **neurotransmitter** expression and promote ciliary neuron survival in cell culture. Previous studies have shown that its biol. effects and biochem. properties are similar to those of ciliary neurotrophic factor (CNTF). In addn., CNTF is present in spinal cord, the source of **MANS**. These observations raised the possibility that **MANS** prepns. contain CNTF. Partially purified **MANS** fractions contain a 24-kD **protein** that is recognized in Western blots by an antiserum generated against recombinant rat CNTF (rCNTF). This antiserum immunoppts. virtually all the cholinergic-inducing and the ciliary neurotrophic activities present in **MANS** prepns. When iodinated rCNTF is incubated with spinal cord membranes, a significant proportion of the labeled CNTF segregates with the membrane pellet. The membrane-assocd. exogenous CNTF can be eluted from the membrane fraction by treatment with high-salt solns., similar to that used to solubilize **MANS** from spinal cord membranes. The data suggest that a substantial portion of the cholinergic differentiation and ciliary neurotrophic activities present in **MANS** prepns. can be attributed to CNTF or a CNTF-like mol.
ST **membrane assocd neurotransmitter stimulating factor** CNTF; ciliary neurotrophic factor **MANS**
IT Animal growth regulators
RL: BIOL (Biological study)
(ciliary neurotrophic **factors, membrane-assocd. neurotransmitter-stimulating factor** cholinergic and ciliary neurotrophic activity dependent on)
IT Animal growth regulators
RL: BIOL (Biological study)
(**membrane-assocd. neurotransmitter-stimulating factors,** cholinergic and ciliary neurotrophic activity of, ciliary neurotrophic **factor**-like mol. in)

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FILE 'HCAPLUS' ENTERED AT 07:35:20 ON 11 MAY 2003
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E MARTIN L/AU
L2 388 S E3,E7
E MARTIN LINDA/AU
L3 23 S E3,E4
E ADLER K/AU
L4 33 S E3,E5
L5 62 S E24-E27
E LI Y/AU
L6 1502 S E3,E16
E LI YUE/AU
L7 178 S E3,E13,E18
L8 32 S E72,E74,E75
L9 2191 S L2-L8
L10 1 S L9 AND MANS
L11 5 S L9 AND MARCKS
L12 5 S L10,L11

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L13          468 S MARCKS(S)(PROTEIN OR ?PEPTIDE?)
L14          467 S MYRIST? ALANINE RICH C KINASE SUBSTRATE
                 E MARCKS
L15          540 S E3
L16           10 S MANS(S)(PROTEIN OR ?PEPTIDE?)
L17            1 S (MANGANESE SENSOR)(L)(PROTEIN OR ?PEPTIDE?)
L18            4 S MEMBRANE ASSOC? NEUROTRANSMIT? STIMULAT?
L19            4 S MEMBRANE(S)ASSOC?(S)NEUROTRANSMIT?(S)STIMULAT?(S)FACTOR
L20         1349 S MEMBRANE(S)ASSOC?(S)FACTOR
L21           57 S MEMBRANE ASSOC? FACTOR
                 SEL DN AN L16 1-6 8
L22            7 S L16 AND E1-E21
L23          571 S L13-L15
L24           67 S L16-L19,L21,L22
                 E MANS
L25          131 S L24 OR E3
L26            5 S L9 AND L23-L25
L27            5 S L12,L26

     FILE 'BIOSIS' ENTERED AT 07:50:02 ON 11 MAY 2003
                 E MARTIN L/AU
L28          813 S E3,E8,E9
                 E MARTIN LINDA/AU
L29           26 S E3,E5
                 E ADLER K/AU
L30          179 S E3,E5
L31           33 S E20-E22
                 E LI Y/AU
L32         2068 S E3,E12,E13
                 E LI YUE/AU
L33           57 S E3,E9,E12
                 E LI YUEH/AU
L34            9 S E5,E7
L35          631 S L23

     FILE 'MEDLINE' ENTERED AT 07:53:21 ON 11 MAY 2003
                 E MARTIN L/AU
L36          898 S E3,E9
                 E MARTIN LINDA/AU
L37            4 S E3,E4
                 E ADLER K/AU
L38          152 S E3,E5
L39            4 S E14
                 E LI Y/AU
L40         3206 S E3,E12
                 E LI YUE/AU
L41           14 S E3,E7
L42          512 S L35

     FILE 'BIOSIS' ENTERED AT 07:54:37 ON 11 MAY 2003

     FILE 'BIOSIS' ENTERED AT 07:55:04 ON 11 MAY 2003
L43          543 S L16-L19,L21 OR MANS
L44            3 S L28-L34 AND L35,L43

     FILE 'MEDLINE' ENTERED AT 07:56:10 ON 11 MAY 2003
L45          131 S L43
L46            1 S L36-L41 AND L42,L45

     FILE 'HCAPLUS, BIOSIS, MEDLINE' ENTERED AT 07:56:54 ON 11 MAY 2003
L47            7 DUP REM L27 L44 L46 (2 DUPLICATES REMOVED)

     FILE 'HCAPLUS, BIOSIS, MEDLINE' ENTERED AT 07:57:12 ON 11 MAY 2003
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L48           6 S L47 NOT ZN2/TI

     FILE 'HCAPLUS, BIOSIS, MEDLINE' ENTERED AT 07:58:12 ON 11 MAY 2003

     FILE 'WPIX' ENTERED AT 07:59:42 ON 11 MAY 2003
L49         347 S L16/BIX OR L17/BIX OR L18/BIX OR L19/BIX OR L21/BIX OR MANS/B
L50           5 S L13/BIX OR L14/BIX OR L15/BIX
                E MARTIN L/AU
L51         107 S E3,E9,E10
                E ADLER K/AU
L52          37 S E3,E4
                E LI Y/AU
L53        3006 S E3,E9
L54           2 S L49,L50 AND L51-L53

     FILE 'WPIX' ENTERED AT 08:03:15 ON 11 MAY 2003
L55           3 S L50 NOT L54
L56         345 S L49 NOT L54
L57           0 S L56 AND (A61P001 OR A61P011 OR A61P043 OR A61P017 OR A61P037)
L58           1 S L56 AND C07K/IC,ICM,ICS,ICA,ICI
L59           3 S L56 AND A61K/IC,ICM,ICS,ICA,ICI
                SEL DN AN 1
L60           1 S L59 AND E1-E2
L61           0 S L56 AND (B04-C01? OR C04-C01? OR B04-N02? OR C04-N02?)/MC
L62           0 S L56 AND (B14-C01 OR C14-C01 OR B12-D01 OR C12-D01 OR B14-C03
L63           1 S L56 AND (B14-C08 OR C14-C08 OR B12-E08 OR C12-D08 OR B14-E10?
L64           0 S L56 AND (B14-L06 OR C14-L06 OR B12-G01 OR C12-G01 OR B14-N17?
L65           5 S L58-L64
L66           1 S L65 AND L60

     FILE 'HCAPLUS' ENTERED AT 08:18:57 ON 11 MAY 2003
L67         701 S L23,L25
L68         696 S L67 NOT L27
                E RESPIRATORY TRACT/CT
L69       15981 S E3-E41
                E E3+ALL
L70      132029 S E4+NT
                E E33+ALL
L71       41854 S E5,E4+NT
L72        1464 S E36+NT OR E37+NT
                E RESPIRAT/CT
L73        8911 S E4+NT
L74        3217 S E39-E43
L75        3217 S E39+NT
                E E94+ALL
L76         119 S E6
                E BRONCHITIS/CT
                E E3+ALL
L77        1797 S E2
L78          28 S E1
                E BRONCH/CT
L79       12161 S E4+NT
L80       12161 S E4-E40
                E ASTHMA/CT
L81       11758 S E3-E5
                E E3+ALL
L82       11758 S E2+NT
                E E4+ALL
L83        7200 S E6,E5+NT
L84        9382 S E4+NT
                E CHRONIC OBSTRUCT/CT
                E E9+ALL
L85        1760 S E2
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                E ULCERATIVE COLITIS/CT
                E E3+ALL
L86         2537 S E2
                E CROHN/CT
                E E5+ALL
L87            0 S E2
                E INFLAMMATORY BOWEL/CT
                E E4+ALL
L88         3655 S E2
                E ROSACEA/CT
                E E3+ALL
L89          137 S E2
                E ECZEMA/CT
L90         1517 S E3,E4
                E E3+ALL
L91         1517 S E7+NT
                E PSORIASIS/CT
L92         6903 S E3-E7
                E E3+ALL
L93         6903 S E4+NT
                E ACNE/CT
L94         2828 S E3-E7
                E E3+ALL
L95         2854 S E4+NT
                E CYSTIC FIBROSIS/CT
                E E3+ALL
L96         5261 S E10,E9+NT
                E ARTHRITIS/CT
L97        12389 S E3-E24
                E E3+ALL
L98        21911 S E6+NT
L99        23165 S E5+NT
                E E19+ALL
L100        4727 S E5,E4+NT
                E E3+ALL
L101       50118 S E4,E5,E3+NT
                E E18+ALL
L102        4920 S E5,E5+NT
                E INFLAMMATION/CT
L103       26292 S E3-E17
                E E3+ALL
L104       79360 S E2+NT
                E SKIN/CT
L105       77777 S E3-E96
                E E3+ALL
L106       83960 S E4+NT
L107        6967 S E34+NT
                E E35+ALL
L108       54406 S E4,E5,E3+NT
                E AUTOIMMUNE/CT
L109       23640 S E7+NT
                E E7+ALL
L110       24266 S E3,E2+NT
                E AUTOIMMUNITY/CT
                E E3+ALL
L111        1638 S E2
                E PAIN/CT
L112        9243 S E3-E11
                E E3+ALL
L113        9094 S E3+NT
L114       91664 S E5+NT OR E6+NT OR E7+NT OR E8+NT OR E9+NT OR E12+NT
                E SECRET/CT
                E E11+ALL
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L115      15601 S E6,E7,E5+NT
                E E4+ALL
L116     282053 S E4+NT
                E MUCIN/CT
                E E13+ALL
L117       5997 S E1
                E MYOSIN/CT
L118      18707 S E4-E32
                E E15+ALL
L119      18283 S E3+NT
L120        131 S L68 AND L69-L119
L121         22 S L120 AND (1 OR 15 OR 63)/SC,SX
L122         24 S L120 AND PATHOL?/SC,SX
L123         40 S L121,L122 NOT L27
L124         34 S L123 AND (PD<=20010626 OR PRD<=20010626 OR AD<=20010626)
L125         29 S L124 AND (PROTEIN OR ?PEPTIDE?)
L126          0 S L125 AND MANS
L127         25 S L125 AND MARCKS
L128          4 S L125 NOT L127
L129          1 S L120 AND MANS
L130        130 S L68 AND L25
L131        116 S L130 AND (PD<=20010626 OR PRD<=20010626 OR AD<=20010626)
L132         19 S L131 AND (1 OR 15 OR 63)/SC,SX
L133         97 S L131 NOT L132
                SEL DN AN 42
L134          1 S L133 AND E1-E3
                SEL DN AN L127 6 8 9 13 14 17 19 21 23 24 25
L135         11 S L127 AND E4-E36
L136         12 S L134,L135 AND L1-L27,L67-L135
L137         12 S L136 AND (MANS OR ?MARCKS?)
L138         12 S L137 NOT L27

     FILE 'HCAPLUS' ENTERED AT 08:45:28 ON 11 MAY 2003
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